



Annual Surveillance Summary: *Pseudomonas aeruginosa* Infections in the Military Health System (MHS), 2016

NMCPHC-EDC-TR-371-2017

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14. ABSTRACT The EpiData Center Department (EDC) conducts routine surveillance of Pseudomonas aeruginosa incidence and prevalence among all beneficiaries seeking care within the Military Health System (MHS). This report describes demographics, clinical characteristics, prescription practices, and antibiotic resistance patterns observed for P. aeruginosa infections in calendar year (CY) 2016. Multiple data sources were linked to assess descriptive and clinical factors related to P. aeruginosa. The overall incidence rate of P. aeruginosa in the MHS beneficiary population decreased and the majority of infections occurred in those over 65 years of age. Regional distribution of infections and drug resistance followed the same trends as in 2015, but with more significant reductions in antibiotic susceptibility. Continued surveillance is recommended.					
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Abstract

The EpiData Center Department (EDC) conducts routine surveillance of *Pseudomonas aeruginosa* incidence and prevalence among all beneficiaries seeking care within the Military Health System (MHS). This report describes demographics, clinical characteristics, prescription practices, and antibiotic resistance patterns observed for *P. aeruginosa* infections in calendar year (CY) 2016.

Multiple data sources were linked to assess descriptive and clinical factors related to *P. aeruginosa*. Health Level 7 (HL7)-formatted Composite Health Care System (CHCS) microbiology data identified *P. aeruginosa* infections. These infections were matched to HL7-formatted CHCS pharmacy data to assess prescription practices, the Standard Inpatient Data Record (SIDR) to determine healthcare-associated exposures, Defense Manpower Data Center (DMDC) rosters to determine burden among Department of Defense (DOD) active duty (AD) service members, and the DMDC Contingency Tracking System (CTS) to determine Department of the Navy (DON) deployment-related infections.

The overall incidence rate of *P. aeruginosa* in the MHS beneficiary population decreased and the majority of infections occurred in those over 65 years of age. Regional distribution of infections and drug resistance followed the same trends as in 2015, but with more significant reductions in antibiotic susceptibility. Continued surveillance is recommended.



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Background, Methods, and Limitations

The EpiData Center (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) prepares a retrospective report each calendar year (CY) that summarizes the demographics, clinical characteristics, prescription practices, and antibiotic susceptibility patterns for *Pseudomonas aeruginosa* infections among Military Health System (MHS) beneficiaries.

Literature review did not provide any new developments or research for *P. aeruginosa* infections. Additionally, no new methods or limitations were applied to this annual summary. As such, this report presents analytical results and discussion of CY 2016 data for *P. aeruginosa* infections in the MHS. The background, methods, and limitations relevant to this analysis have been discussed in a previous report (CY 2015 annual report for *P. aeruginosa*¹).

The EDC also monitors other multidrug-resistant organisms (MDROs) of interest in the MHS.^{2,3}



Results

Section A – Descriptive Epidemiology

Incidence of *P. aeruginosa*

In 2016, the annual incidence rate (IR) for *P. aeruginosa* infection among MHS beneficiaries treated at a military treatment facility (MTF) was 31.8 per 100,000 persons per year (Table 1). This reflects a 2.8% change above the weighted historic IR. Incidence rates in the Army and Navy beneficiary populations increased, while rates in the Air Force beneficiary, Marine Corps beneficiary, and Department of Defense (DOD) active duty (AD) populations decreased. The greatest percent change, as well as the highest incidence, was seen in the Marine Corps beneficiary population, where the IR dropped 8.0% below the historic IR to 29.7 per 100,000 persons per year. All 2016 IRs were within two standard deviations of the weighted historic IRs.

Table 1. Incidence Rate (IR) for *P. aeruginosa* Infections in the MHS, CY 2016

Population	2016 IR	Weighted Historic ^a IR 2013 - 2015	Two Standard Deviations: Weighted Historic ^a IR	2016	
				Direction	Percent Change ^b
MHS	31.8	30.9	4.9	↑	2.8%
Air Force	26.0	27.1	5.1	↓	4.2%
Army	28.9	27.9	4.5	↑	3.7%
Marine Corps	29.7	32.3	7.3	↓	8.0%
Navy	28.8	27.8	4.0	↑	3.6%
DOD Active Duty	26.4	28.2	3.5	↓	6.6%

Rates are presented as the rate per 100,000 persons per year.

A green arrow indicates an increasing percent change and a blue arrow indicates a decreasing percent change.

^a Historic IR reflects the weighted average of the three years prior to the analysis year.

^b This reflects the percent change from the weighted historic IR to the IR of the current analysis year.

Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.



Demographic Distribution of *P. aeruginosa*

In 2016, there were 2,988 incident *P. aeruginosa* infections identified among all MHS beneficiaries treated at an MTF. The highest incidence rates among each demographic category occurred in males, retired service members, and those over the age of 65 (Table 2).

Table 2. Demographic Characteristics of *P. aeruginosa* Infections in the MHS, CY 2016

	N = 2,988	
	Count	Rate
Gender		
Female	1,335	28.9
Male	1,653	34.5
Age Group (in Years)		
0-17	504	25.7
18-24	237	20.7
25-34	275	22.9
35-44	204	24.4
45-64	659	32.1
65+	1,109	50.0
Beneficiary Type		
Active Duty	360	26.4
Family Members	1,480	27.0
Retired	708	32.4
Other ^a	440	--

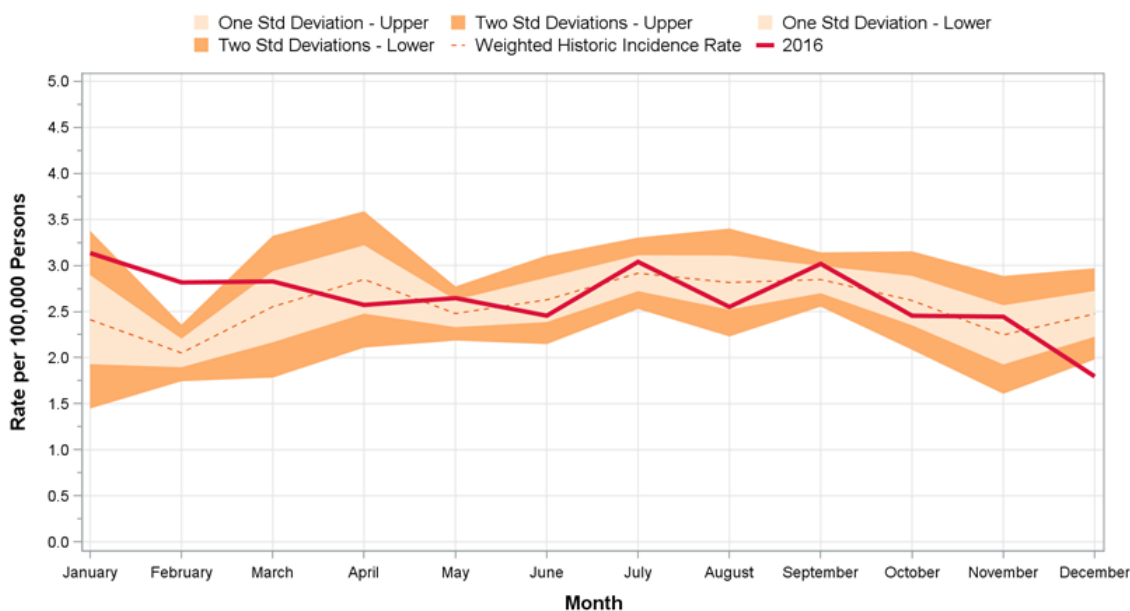
^a Rate is not reported due to variation in population denominator.
 Rates are presented as the rate per 100,000 persons per year.
 Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
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Seasonality

Monthly incidence rates of *P. aeruginosa* infections in 2016 were stagnant from March through November, all ranging between 2.5 to 3.0 per 100,000 persons per year (Figure 1). February and December's IRs were outside the expected variance of two standard deviations from the weighted historic IR. February's IR was 2.8 per 100,000 persons per year and above the historic IR of 2.0 per 100,000 persons per year. December's IR was 1.7 per 100,000 persons per year and below the historic IR of 2.6 per 100,000 persons per year. These two data points combined with the stagnant IRs the rest of the year highlight the lack of a seasonal trend for *P. aeruginosa* for 2016.

Figure 1. Monthly Incidence of *P. aeruginosa* Infections and Weighted Historic Incidence Rate (IR) Comparisons in the MHS, CY 2016



Rates are presented as the rate per 100,000 persons per year.

Bands indicate one and two standard deviations above and below the weighted historic monthly incidence rates (IR).

The weighted historic monthly IR is a weighted average of the three years prior to the analysis year.

Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

P. aeruginosa Clinical Characteristics

There were 3,500 prevalent *P. aeruginosa* infections identified among all MHS beneficiaries treated at an MTF in 2016. The infection burden was higher in the outpatient setting (79.7%) and generally presented as non-invasive infections (92.5%) (Table 3). The majority of *P. aeruginosa* infections were collected from urine specimens (37.3%); 29.0% were collected from respiratory specimens and 21.1% were collected from skin and soft tissue infections (SSTIs) or wounds.

Table 3. Clinical Characteristics of *P. aeruginosa* Prevalent Infections in the MHS, CY 2016

	N = 3,500	
	Count	Percentage
Specimen Collection Location		
Inpatient	709	20.3
Outpatient	2,791	79.7
Infection Type		
Invasive	263	7.5
Non-Invasive	3,237	92.5
Body Collection Site		
Blood	64	1.8
Respiratory	1,014	29.0
SSTI/Wound	740	21.1
Urine	1,305	37.3
Other	377	10.8

Data Source: NMCPHC HL7-formatted CHCS microbiology database.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.



Exposure Burden Metrics

Table 4 presents two different metrics describing the burden of multidrug-resistant organism (MDRO) infection rates for healthcare-associated exposures. In 2016, there were 239,946 direct care inpatient admissions across all MHS MTFs. The overall MDRO prevalence rate for *P. aeruginosa* was 0.9 per 1,000 inpatient admissions; this metric measures the exposure of infection at any point during the admission or one year prior. Within the United States (US), the South region had the highest overall MDRO prevalence rate (2.0 per 1,000 inpatient admissions). The admission MDRO prevalence rate for *P. aeruginosa* was 0.7 per 1,000 inpatient admissions; this metric measures the magnitude of infection at the time of admission (importation of MDRO into the healthcare system) or one year prior. As with overall MDRO prevalence, within the US, the South region had the highest admission MDRO prevalence rate (1.6 per 1,000 inpatient admissions). Among *P. aeruginosa* infections, the overall MDRO prevalence rate was higher than the admission MDRO prevalence rate (0.9 vs. 0.7 per 1,000 inpatient admissions), but close in rate; this observation suggests that the majority of *P. aeruginosa* infections were imported into the hospital setting from the community, adding to the burden of *P. aeruginosa*.

Table 4. MDRO Healthcare-Associated Exposure Burden Metrics among *P. aeruginosa* in the MHS, CY 2016

	Overall MDRO Prevalence ^a		Admission MDRO Prevalence ^b	
	Count	Rate ^c	Count	Rate ^c
Region				
OCONUS	6	0.3	4	--
US Midwest	2	--	1	--
US Northeast	0	--	0	--
US South	113	2.0	92	1.6
US South Atlantic	65	0.8	54	0.7
US West	34	0.5	26	0.3
Total	220	0.9	177	0.7

^a Overall MDRO prevalence included all individuals with an MDRO infection identified from a sample collected at any point during the admission, as well as samples that tested positive for infection in the prior calendar year.

^b Admission MDRO prevalence included all individuals with an MDRO infection identified from samples collected up to and including the third day of admission, as well as samples that tested positive for infection in the prior calendar year.

^c Rates are presented as the rate per 1,000 inpatient admissions per year. Rates are not provided when the prevalence count is less than or equal to 5.

Data Source: NMCPHC HL7-formatted CHCS microbiology and SIDR databases.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

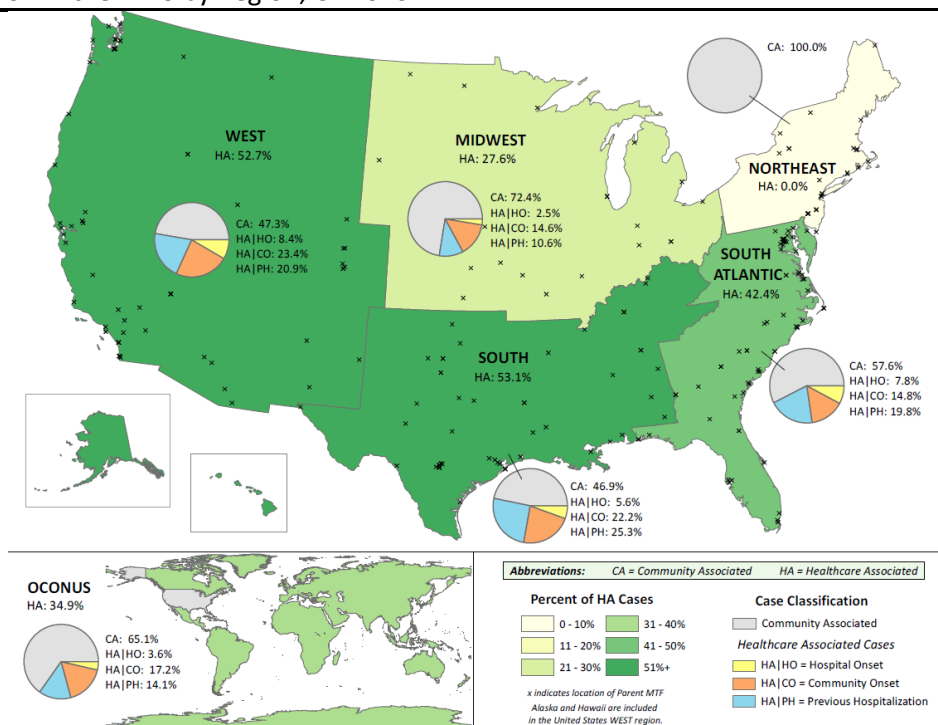


Regional Epidemiologic Infection Classifications

Among all prevalent *P. aeruginosa* infections identified in the MHS in 2016, 52.6% were community-associated (CA) cases and 47.4% were healthcare-associated (HA) cases. Regionally, the US South reported the highest proportion of HA *P. aeruginosa* cases (53.1%), followed by the US West (52.7%), US South Atlantic (42.4%), locations outside of the continental United States (OCONUS) (34.9%), and US Midwest (27.6%). There were no HA *P. aeruginosa* cases in the US Northeast (Figure 2).

HA cases were further categorized into hospital-onset (HO), community-onset (CO), or previous hospitalization (PH) groupings. Of all *P. aeruginosa* cases regardless of regional location, 20.0% were CO cases, indicating that the infection most likely originated from the community. Only 6.8% of all *P. aeruginosa* cases were HO, indicating that the infection was most likely contracted during the current hospitalization. Regionally, the US West and US South displayed similar patterns with HA *P. aeruginosa*. Both had over half of their *P. aeruginosa* cases categorized as HA, with most being CO or PH. The US West had the largest percentage of HO cases at 8.4% and the US South had the largest percentage of PH cases at 25.3%. While the US South Atlantic did not have the largest percentage of HA *P. aeruginosa* cases, it did have the second largest percentage of HO *P. aeruginosa* cases at 7.8%.

Figure 2. Proportion of Healthcare- and Community-Associated Cases among *P. aeruginosa* Infection in the MHS by Region, CY 2016



Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
 Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.



Section B – Antimicrobial Resistance and Use

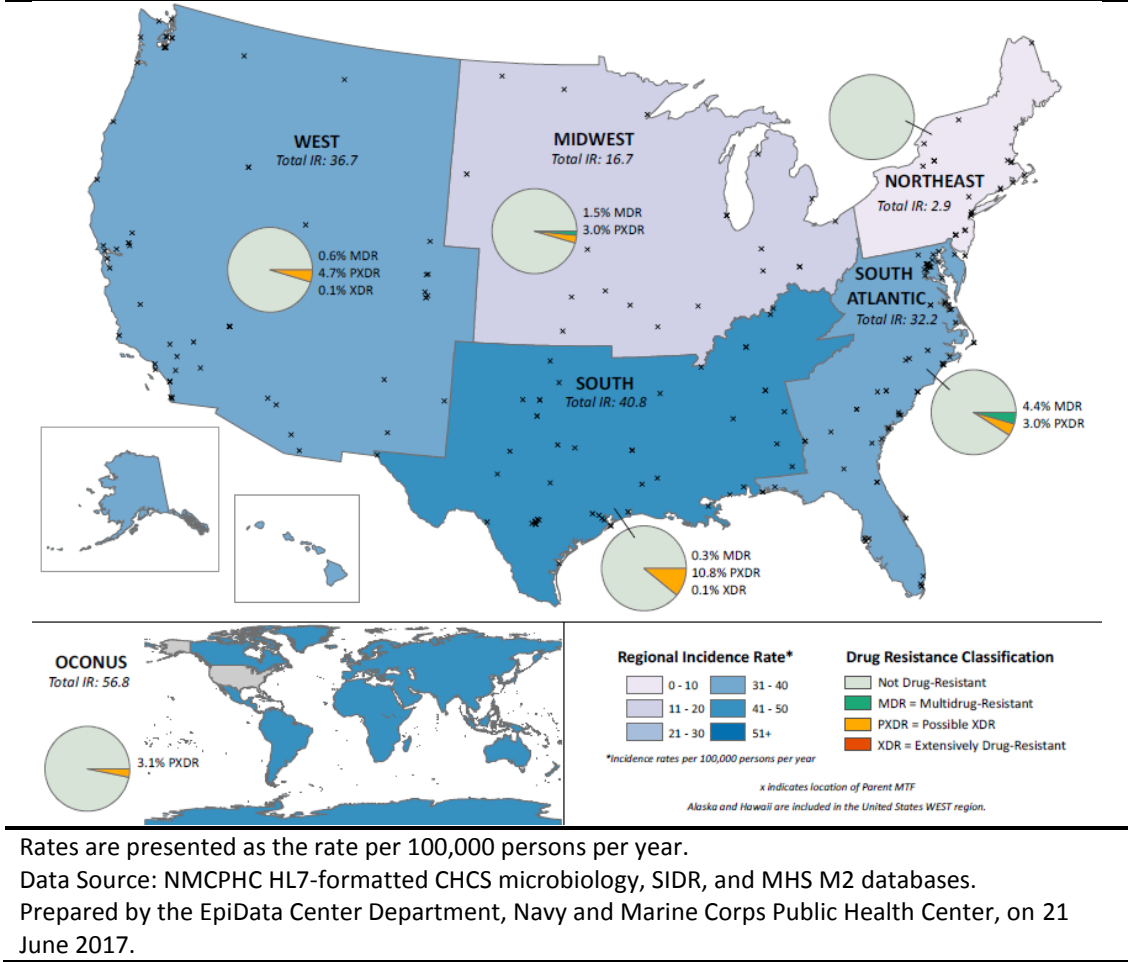
Regional Multidrug Resistance

The 2016 annual incidence rate of *P. aeruginosa* among all MHS beneficiaries was 31.8 per 100,000 persons per year; the IR of drug-resistant *P. aeruginosa* infection (i.e., resistant to antibiotics in at least three classes) was 1.9 infections per 100,000 persons per year. Regionally, the highest incidence rates occurred in OCONUS locations (56.8 per 100,000 persons per year), followed by the US South region (40.8) and the US West region (36.7) (Figure 3). The lowest incidence rate was observed in the US Northeast region at 2.9 per 100,000 persons per year.

About 8.1 percent of all prevalent *P. aeruginosa* infections in the MHS were multidrug-resistant (MDR), extensively drug-resistant (XDR) or possibly XDR (PXDR). The US South region had the greatest percentage of drug-resistant *P. aeruginosa* infections with 0.3% MDR, 10.8% PXDR, and 0.1% XDR. The US South Atlantic had the next highest percentage of drug-resistant *P. aeruginosa* with 4.4% MDR and 3.0% PXDR. The US Northeast region did not have any multidrug-resistant *P. aeruginosa* infections.



Figure 3. Annual Incidence Rate (IR) and Percentage of Multidrug Resistance among *P. aeruginosa* Infections in the MHS by Region, CY 2016



Antibiogram

Table 5 displays an antibiogram of *P. aeruginosa* incident infections for all MHS beneficiaries from 2011-2016. In 2016, *P. aeruginosa* infections were most susceptible to doripenem (98.8%), colistin (97.3%), and tobramycin (96.1%). Infections were least susceptible to ticarcillin/clavulanate (46.7%) and aztreonam (78.3%). Statistically significant increasing trends in susceptibility were observed for gentamicin and tobramycin, while statistically significant decreasing trends in susceptibility were seen in imipenem, meropenem, piperacillin/tazobactam, and ticarcillin/clavulanate.

Table 5. Antibiogram of *P. aeruginosa* Infections Identified in the MHS, CY 2011-2016

Antibiotics	2011	2012	2013	2014	2015	2016	Susceptibility Trend	Comment ^a
Amikacin	94.0%	95.1%	94.2%	94.8%	95.0%	94.9%	100.0% 90.0%]	
Aztreonam	77.1%	77.4%	78.4%	76.6%	79.4%	78.3%	80.0% 70.0%]	
Cefepime	92.3%	93.5%	93.5%	93.4%	92.7%	93.3%	100.0% 90.0%]	
Ceftazidime	95.1%	95.2%	94.7%	94.6%	94.8%	93.9%	100.0% 90.0%]	
Ciprofloxacin	87.1%	88.8%	86.8%	88.5%	87.5%	88.6%	90.0% 80.0%]	
Colistin	93.7%	98.8%	97.3%	95.1%	95.4%	97.3%	100.0% 90.0%]	
Doripenem	100.0%	100.0%	100.0%	97.5%	95.2%	98.8%	100.0% 90.0%]	
Gentamicin	87.0%	90.7%	90.5%	89.3%	91.3%	91.6%	95.0% 85.0%]	↑
Imipenem	92.4%	92.3%	90.2%	90.3%	90.6%	89.6%	95.0% 85.0%]	↓
Levofloxacin	84.4%	86.8%	84.9%	86.9%	84.8%	85.7%	90.0% 80.0%]	
Meropenem	93.8%	93.6%	94.2%	93.8%	92.2%	91.0%	95.0% 85.0%]	↓
Piperacillin	92.6%	96.1%	96.3%	93.5%	95.2%	95.7%	100.0% 90.0%]	
Piperacillin/Tazobactam	95.8%	94.2%	94.4%	93.6%	93.5%	93.2%	100.0% 90.0%]	↓
Ticarcillin/Clavulanate	85.6%	84.2%	50.0%	42.0%	63.1%	46.7%	90.0% 40.0%]	↓
Tobramycin	94.8%	96.4%	95.4%	95.3%	95.0%	96.1%	100.0% 90.0%]	↑

‘--’ indicates that fewer than 30 isolates were tested.

^a Arrow indicates the antibiotics with a significant change in direction of trend for significant two-tailed Cochrane-Armitage tests for trend established for a single antibiotic over time. A significant increase in susceptibility is denoted by a green upward arrow and a significant decrease in susceptibility is denoted by a blue downward arrow.

Data Source: NMCPHC HL7-formatted CHCS microbiology database.

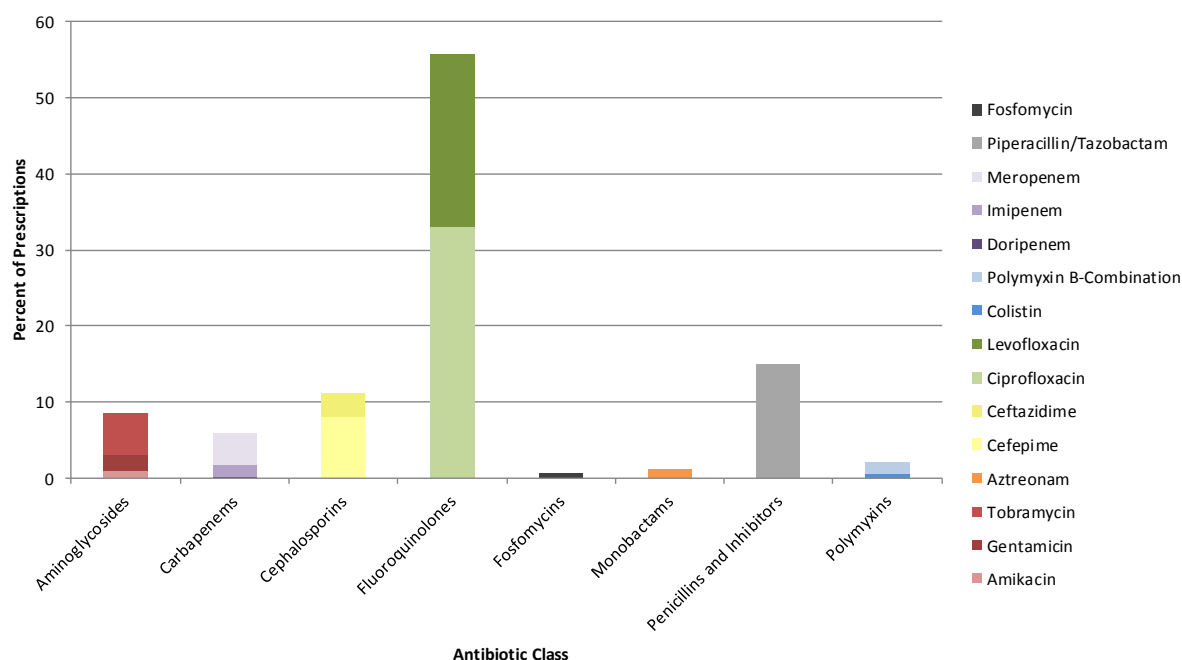
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Antimicrobial Consumption/Prescription Practices

Among all MHS beneficiaries, the most commonly prescribed antibiotics associated with *P. aeruginosa* infections in 2016 were the fluoroquinolones ciprofloxacin (33.0%) and levofloxacin (22.7%), followed by piperacillin/tazobactam (15.0%) (Figure 4). The next most frequently prescribed class of antibiotics was cephalosporins (11.1%), of which cefepime attributed 8.2% of all prescriptions.

Figure 4. *P. aeruginosa* Infection and Prescription Practices in the MHS, CY 2016



Only the first occurrence of a unique antibiotic was counted per person per infection, regardless of administration route.

Data Source: NMCPHC HL7-formatted CHCS microbiology and HL7-formatted pharmacy databases.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Section C – Special Populations

Of the 3,500 prevalent *P. aeruginosa* infections in the MHS in 2016, less than 0.1% (N = 8) occurred among Department of the Navy (DON) AD deployed personnel. Of these deployment-related *P. aeruginosa* infections, all beneficiaries were male and most (75%) were between 18 and 34 years of age.



Discussion

The incidence of *P. aeruginosa* in the MHS increased in 2016 compared to the historical average. Unlike in 2015,¹ not all beneficiary population IRs increased compared to the historic IRs, which might suggest that the increasing trend in incidence is stabilizing. In 2015, the incidence rate in the MHS increased 13.8% from the historical IR, while in 2016 it only increased 2.8%. The Air Force, Marine Corps, and DOD AD population IRs decreased 4-8%, but were within an expected variance of two standard deviations. Similar to 2015, the incidence rate in those over the age of 65 was almost double the incidence rate of any other age group.

P. aeruginosa is an opportunistic gram-negative bacterium, expected to affect the immunocompromised the most. It tends to target the very young and elderly populations, as well as those in a hospital setting. A little over a fifth of the MHS *P. aeruginosa* infections in 2016 were identified in an inpatient setting. Similar to 2015, 47% of all prevalent *P. aeruginosa* infections were found to be HA. Over half of the prevalent *P. aeruginosa* infections found in the US West and US South regions were HA. This higher percentage could be attributed to the large number of MTFs found in these regions, providing more exposure to a hospital environment compared to the other US and OCONUS regions.

A growing concern both in and outside of the hospital setting is the rise of multidrug-resistant *P. aeruginosa* infections. In the MHS in 2016, 8.1% of all prevalent *P. aeruginosa* infections were multidrug-resistant, and most of these were classified as PXDR. The antibiogram for 2016 showed there were no antibiotics to which *P. aeruginosa* infections were 100% susceptible. Differing from 2015, the carbapenems imipenem and meropenem both showed a statistically significant decrease in efficacy in the MHS. Imipenem displayed less than 90% efficacy for the first time in the MHS, and meropenem is close to doing the same.

Ciprofloxacin and levofloxacin, both fluoroquinolones, accounted for over 50% of all prescriptions associated with *P. aeruginosa* infections in the MHS, but both had an efficacy of less than 90%. The next most frequently prescribed antibiotic, piperacillin/tazobactam, had an efficacy of over 90% but a statistically significant decreasing trend for 2016. The cephalosporins cefepime and ceftazidime were the next most frequently prescribed, and both had an efficacy of more than 90%, with no statistically significant change or trend for 2016. These findings suggest the fluoroquinolones are being used as the first line of defense, but are likely followed by piperacillins and cephalosporins due to their greater efficacy. The use and significantly decreasing efficacy of piperacillin/tazobactam should continue to be monitored.

Due to the decreasing efficacy of relevant antibiotics, the rise of MDR *P. aeruginosa*, and the resilient nature of the organism, continued surveillance of *P. aeruginosa* is recommended. Further understanding of how *P. aeruginosa* affects the MHS population is needed to continue to curb the rising incidence trend. Going forward, the cystic fibrosis (CF) patient population within the MHS should be identified and analyzed. *P. aeruginosa* is the most significant pathogen in CF and infects 60% of all CF patients.⁴ A sub-analysis would describe how this population is influencing the incidence of *P. aeruginosa* in the MHS and provide a more concrete understanding of its effect within the non-CF patient population.



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Appendix A: Antibiotics Included in Resistance Definitions

Table A1: Antibiotics Included in the Resistance Definitions for *P. aeruginosa* Infections in the DOD, CY 2015

Antibiotic Class	Antibiotics Included in Class
Aminoglycosides	Gentamicin
	Tobramycin
	Amikacin
	Netilmicin
Carbapenems	Imipenem
	Meropenem
	Doripenem
Cephalosporins	Ceftazidime
	Cefepime
Fluoroquinolones	Ciprofloxacin
	Levofloxacin
Penicillins + β -lactamase inhibitors	Ticarcillin-clavulanic acid
	Piperacillin-tazobactam
Monobactams	Aztreonam
Phosponic acids	Fosfomycin
Polymyxins	Colistin
	Polymyxin B

Source: Magiorakos et al., 2012.

Prepared by the EpiData Center Department, Navy and Marine Corps
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Appendix B: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
AD	active duty
CA	community-associated
CF	cystic fibrosis
CHCS	Composite Health Care System
CTS	Contingency Tracking System
CY	calendar year
DOD	Department of Defense
DON	Department of the Navy
EDC	EpiData Center Department
HA	Healthcare-associated
HL7	Health Level 7
HO	hospital-onset
IR	incidence rate
MDR	multidrug-resistant
MDRO	multidrug resistant organism
MHS	Military Health System
NMCPHC	Navy and Marine Corps Public Health Center
PH	previous hospitalization
PXDR	possible extensively drug-resistant
SSTI	skin and soft tissue infection
XDR	extensively drug resistant

